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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| EXAMINER | |
|---|---|
| JIANG, SHAOJIA A | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1617 | |

DATE MAILED: 09/19/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/766,749 | KNUTSON ET AL. | |
| | Examiner | Art Unit | |
| | Shaojia A. Jiang | 1617 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *15 August 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *13 and 15-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13 and 15-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

This Office Action is in response to Applicant's amendment and response filed on August 15, 2005, wherein claims 13 and 15-20 have been amended since claim 13 has been amended. Claims 1-12 and 14 are cancelled previously.

Claims 13 and 15-20 as amended now are examined on the merits herein, however the amendment does not comply with 37 CFR 1.173(b). A proper amendment must be submitted in response to this Action.

Applicant's amendment filed August 15, 2005 with respect to the rejection of claims 13 and 15-20 made under 35 U.S.C. 112 first paragraph for containing new subject matter which was not described in the original specification and claims, i.e., "non-oral dosage form" of record stated in the Office Action dated March 11, 2005 have been fully considered and found persuasive to remove the rejection since the recitation "non-oral dosage form" has been removed from the claims. Therefore, the said rejection is withdrawn.

### *Claim Rejections - 35 USC § 251*

The reissue oath/declaration filed with this application is defective because it fails to identify at least one error which is relied upon to support the reissue application. See 37 CFR 1.175(a)(1) and MPEP § 1414. This rejection is of record stated in the Office Action dated March 11, 2005.

Claim 13 and 15-20 are rejected as being based upon a defective reissue oath/declaration under 35 U.S.C. 251 as set forth above. See 37 CFR 1.175.

The nature of the defect(s) in the oath/declaration is set forth in the discussion above in this Office action, e.g., the statement "[t]his application for reissue is based on at least the error that the full breadth of claim 1 is not supported in accord with the written description requirement of 35 U.S.C. § 112, first paragraph, by the specification of the patent as filed" in the Application Declaration by the Assignee is not considered to specifically identify at least one error which is relied upon to support the reissue application.

***Response to Argument***

Applicant's arguments filed August 15, 2005 with respect to this rejection of record in the previous Office Action March 11, 2005 have been fully considered but are not deemed persuasive as further discussed below.

Applicants assert that "[i]n order to satisfy the requirements of 35 USC 251 and 37 CFR 1.175, Applicants submitted a Declaration on January 28, 2004 stating the error was that the patentee claimed more than they had a right to claim in claim 1 of the application under 35 USC 112, first paragraph.

The relevant portion of the Declaration recites:

"..this application for reissue is based on at least the error that the full breadth of claim 1 is not supported in accord with the written description requirement of 35 USC 112, first paragraph, by the specification of the patent as filed." See Applicants' remarks at page 5.

However, the Application Declaration is not considered to specifically identify at least one error which is relied upon to support the reissue application, i.e., it is unspecific or unclear as to which is not supported by the written description, e.g., the full breadth of the medical conditions or disease states, or the vitamin D compounds encompassed thereby, or both, which the patentee claimed more than they had a right to claim in claim 1 of the application under 35 USC 112, first paragraph.

For the above stated reasons, said claims are properly rejected under 35 U.S.C. 251. Therefore, said rejection is adhered to.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 13 and 15-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over DeLuca, Hector F. (US 4,225,596) in view of Sakhaee et al. ("Postmenopausal osteoporosis as a manifestation of renal hypercalciuria with secondary hyperparathyroidism") and Applicant's admission regarding the prior art in the specification (see 5,861,386, "Background of the Invention" at col.1 line 18-24), of record in the Office Action dated March 11, 2005.

DeLuca discloses that the vitamin D compound having the structural formula therein such as the instant compound, 1α-hydroxyergocalciferol (see col.3 line 22) also known as 1α-hydroxy-vitamin $D_2$ or 1α-OH-vitamin $D_2$ (see chemical name provided by ACS on STN, PTO-892), is useful in a method for treating or preventing the depletion of calcium from the bones of women entering menopause or who are postmenopausal (see col.1 lines 18-22 and 50-51), and a method for increasing the calcium absorption and retention within the body of mammals including humans displaying evidence of, or having a physiological tendency to ward, loss of bone mass, by administering 1α-hydroxyergocalciferol to a human in need thereof such as a postmenopausal woman (see claims 1-5 in particular).

DeLuca discloses that the doses of the instant vitamin D for the methods of the treatment therein are from about 0.1-1 μg (microgram) per day (see col.3 line 30-31). Thus, the dosage amount for a week is (0.1-1 μg per day) X 7 days = 0.7-7 μg per week, which overlaps or within the claimed range. DeLuca discloses the specific parenteral form of the 1α-OH-vitamin $D_2$ composition such as by injection or intravenously or by alimentary canal (see col.3 line 28-30).

DeLuca also teaches that other vitamin D compounds, calcium supplement (also known calcium-based phosphate binder), estrogens, fluoride (known as to be administered as sodium fluoride) alone or in combination, are known to be used in the methods of treating bone disorders characterized by loss of bone mass, in particular, postmenopausal osteoporosis (see col.1 line 23-61).

DeLuca does not expressly disclose the employment of the 1α-OH-vitamin $D_2$ composition in a method for lowering elevated or maintaining lowered serum parathyroid hormone levels in the human suffering from hyperparathyroidism secondary to end stage renal disease. DeLuca does not expressly disclose that the vitamin $D_2$ to be given 1 to 3 times per week.

Sakhaee et al. teaches postmenopausal osteoporosis as a manifestation of renal hypercalciuria with secondary hyperparathyroidism in postmenopausal women (see the abstract in particular).

Moreover, Applicant clearly admits and acknowledges in the specification regarding the prior art that it is known that "renal osteodystrophy is encountered in end-stage renal disease patients undergoing chronic dialysis (see 5,861,386, "Background of the Invention" at col.1 line 18-24).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to employ the 1α-OH-vitamin $D_2$ composition in a method for lowering elevated or maintaining lowered serum parathyroid hormone levels in the human suffering from hyperparathyroidism secondary to end stage renal disease in a human in need thereof, e.g., a postmenopausal woman, and to schedule or program the regimen by administering the vitamin $D_2$ 1 to 3 times per week in the known amount of the prior art.

One having ordinary skill in the art at the time the invention was made would have been motivated to employ the 1α-OH-vitamin $D_2$ composition in a method for lowering elevated or maintaining lowered serum parathyroid hormone levels in the

human suffering from hyperparathyroidism secondary to end stage renal disease in a human in need thereof, e.g., a postmenopausal woman, since postmenopausal osteoporosis as a manifestation of renal hypercalciuria with secondary hyperparathyroidism is known to be encountered in postmenopausal women according to Sakhaee et al. Moreover, it is known before the invention herein made that "renal osteodystrophy is encountered in end-stage renal disease patients undergoing chronic dialysis" according to Applicant's admission in the specification.

Thus, the pathological conditions related to the depletion of calcium from the bones of women entering menopause or who are postmenopausal and/or in need of increasing the calcium absorption and retention within the body of mammals including humans displaying evidence of, or having a physiological tendency to ward, loss of bone mass, e.g., in postmenopausal women, taught by DeLuca, would clearly encompass pathological conditions, hyperparathyroidism secondary to end stage renal disease in a human in need thereof as claimed herein, e.g., in a postmenopausal woman.

Therefore, the patient population in DeLuca is deemed to encompass or overlap or coincide the patient herein having osteoporosis and suffering from hyperparathyroidism secondary to end stage renal disease in need of lowering elevated or maintaining lowered serum parathyroid hormone levels.

Therefore, one of ordinary skill in the art would have reasonably expected that 1α-OH-vitamin $D_2$, would have beneficial therapeutic effects and usefulness in a method for lowering elevated or maintaining lowered serum parathyroid hormone levels in the

human suffering from hyperparathyroidism secondary to end stage renal disease, e.g., a postmenopausal woman, to treat hyperparathyroidism secondary to end stage renal disease, by administering the same effective amounts of the same compound of DeLuca to the same or overlapping patient population.

Additionally, scheduling or programming a regimen by administering the vitamin $D_2$ 1 to 3 times per week, or once or twice a day, based on the known amount of the prior art is deemed obvious since they are all within the knowledge and conventional skills of pharmacologist or a medical practitioner.

Thus the claimed invention as a whole is clearly prima facie obvious over the teachings of the prior art.

***Response to Argument***

Applicant's arguments filed August 15, 2005 with respect to the rejection made under 35 U.S.C. 103(a) in the previous Office Action March 11, 2005 have been fully considered but are not deemed persuasive as to the nonobviousness of the claimed invention over the prior art as further discussed below.

Applicants assert that "there is no motivation or suggestion to modify or combine the references with reasonable expectation of success and the references fail to teach or suggest all the claim limitations."

Contrary to Applicants' assertion, as discussed in the previous Office Action, postmenopausal osteoporosis as a manifestation of renal hypercalciuria with secondary hyperparathyroidism is known to be encountered in postmenopausal women according to Sakhaee et al. Moreover, it is also known before the invention herein made that

"renal osteodystrophy is encountered in end-stage renal disease patients undergoing chronic dialysis".

Thus, the pathological conditions related to the depletion of calcium from the bones of women entering menopause or who are postmenopausal and/or in need of increasing the calcium absorption and retention within the body of mammals including humans displaying evidence of, or having a physiological tendency to ward, loss of bone mass, e.g., in postmenopausal women, taught by DeLuca, would clearly encompass pathological conditions, hyperparathyroidism secondary to end stage renal disease in a human in need thereof as claimed herein, e.g., in a postmenopausal woman.

Therefore, the patient population in DeLuca is deemed to encompass or overlap or coincide the patient herein having osteoporosis and suffering from hyperparathyroidism secondary to end stage renal disease in need of lowering elevated or maintaining lowered serum parathyroid hormone levels.

Therefore, one of ordinary skill in the art would have reasonably expected that administering the same effective amounts of the same compound, 1α-OH-vitamin $D_2$, of DeLuca to the **same** patient, a postmenopausal woman, for treating the depletion of calcium from the bones of women entering menopause or who are postmenopausal, and for increasing the calcium absorption and retention within the body of mammals including humans displaying evidence of, or having a physiological tendency to ward, loss of bone mass, would have lowered elevated or maintained lowered serum parathyroid hormone levels in said postmenopausal woman also suffering from

hyperparathyroidism secondary to end stage renal disease, e.g., , to treat hyperparathyroidism secondary to end stage renal disease, with reasonable expectation of success, .

Note that absolute certainty and conclusion are not required as a basis of a rejection under 35 U.S.C. 103 for obviousness. Absolute predictability is not required, only a reasonable expectation of success. See *In re Lamberti and Konort*, 192 USPQ 278.

One cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. In re Keller, 642 F.2d 413, 208 SPQ 871 (CCPA 1981); In re Merck & Co., Inc., 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). See MPEP 2145. Therefore, the motivation to combine the teachings of the prior art cited herein to make the present invention is seen. The claimed invention is clearly obvious in view of the prior art.

For the above stated reasons, said claims are properly rejected under 35 U.S.C. 103(a). Therefore, said rejection is adhered to.

In view of the rejections to the pending claims set forth above, no claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Jiang, whose telephone number is (571)272-0627. The examiner can normally be reached on Monday-Friday from 9:00 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, Ph.D., can be reached on (571)272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

S. Anna Jiang, Ph.D.
Primary Examiner
Art Unit 1617
September 14, 2005